employed by the authors, neither psychomotor nor mental development was affected by smoke exposure during pregnancy and early infancy. Infections of the lower respiratory tract were more frequent in the children of smoking mothers. These mothers weaned their babies earlier than non-smokers, but the different feeding behaviour did not influence any of the clinical parameters that were investigated in this study. In order to evaluate the extent of smoke exposure, cotinine was measured in children's urine and in breast milk once a month throughout the first year of life. Cotinine in the urine was significantly dependent on feeding behaviour: infants breast fed showed concentrations 10-fold higher than those who were bottle fed. Cotinine excretion in urine of infants from smoking mothers, who were not breast fed (nicotine exposure via passive smoking only) was even higher than that of adult passive smokers. If infants from smoking mothers were breast fed, their urinary cotinine excretion was in the range of adult smokers.(ABSTRACT TRUNCATED AT 250 WORDS)

5/AU,TI,SO,AB/33 (Item 33 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

The role of vasopressin in the nicotine-induced stimulation of ACTH and cortisol in men.
Stalke J; Hader O; Bahr V; Hensen J; Scherer G; Oelkers W
Clin Investig Mar Apr 1992, 70 (3-4) p218-23,
Experimental evidence indicates that arginine vasopressin (AVP) contributes to the release of ACTH under certain conditions. The present study investigates the role of vasopressin as a secretagogue of ACTH during cigarette smoking or nicotine infusion with additional injection of corticotropin releasing hormone (CRH) and using the specific AVP antagonist d(CH2)5Tyr(Me)-AVP. We first tested the effect of the AVP antagonist (10 micrograms/kg body weight i.v.) on ACTH and cortisol release following cigarette smoking in 15 healthy young male smokers. Smoking led to marked increments in plasma nicotine and to a small rise in plasma ACTH and cortisol. Mean plasma ACTH and cortisol levels were at no time significantly altered by the antagonist. This might be due to a slight agonistic effect of the AVP antagonist, to high interindividual variability of the ACTH and cortisol responses after smoking or to a negligible role of AVP in smoking-induced ACTH release. In a second study we performed the following tests in six healthy male non-smokers: (1) nicotine infusion (1.0 micrograms/kg body weight per min); (2) CRH i.v. (100 micrograms); (3) AVP antagonist i.v. (5 micrograms/kg); (4) nicotine infusion plus CRH i.v.; (5) nicotine infusion plus AVP antagonist i.v.; (6) nicotine infusion plus CRH and AVP antagonist i.v.; and (7) sham infusion. Nicotine infusion led to greater increments of AVP, ACTH and cortisol than smoking without causing nausea. Peak nicotine levels after nicotine infusion were lower than after smoking. The AVP antagonist in the reduced dosage given alone had no effect on hormone levels. However, it slightly attenuated the effect of nicotine on ACTH and cortisol (P less than 0.05, ANOVA).(ABSTRACT TRUNCATED AT 250 WORDS)

5/AU,TI,SO,AB/34 (Item 34 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Smoking habits in relapsed subjects from a smoking cessation trial after one year.
Norregaard J; Tonnesen P; Simonsen K; Petersen L; Gawe U
Br J Addict Aug 1992, 87 (8) p1189-94,
Reports of smoking cessation studies often claim that many relapsed subjects reduce their smoking. We investigated the smoking habits of

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relapsers 1 year after quitting in a smoking cessation trial using nicotine or placebo patches. All 280 participants in that study were summoned to a 1-year follow-up visit. 148 (57%) of 259 relapsers attended, as did all 30 sustained abstainers. Fewer than 1% of the subjects had quit spontaneously after the primary relapse. Daily cigarette consumption, standard nicotine yield per cigarette, saliva cotinine concentration, expired carbon monoxide level and two nicotine dependency scales were assessed at entry and at the 1-year follow-up. In five of these six smoking-related characteristics, there was a small but significant mean reduction of 7%-27%. A significant weight gain of 0.5 +/- 2.9 kg (mean +/- SD) was recorded in the relapsers compared with 1.8 +/- 4.2 kg for abstainers (p less than 0.001). It is concluded that smoking habits in relapsers are relatively unchanged, and thus the most important outcome measure in smoking cessation trials is abstinent subjects.

5/AU,TI,SO,AB/35 (Item 35 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Haemodynamic effects of a new dihydropyridine calcium entry blocker, S-12968-(-), in a rat model of cardiovascular calcium overload.

Makki T; Lartaud I; Bray des Boscs L; Capdeville Atkinson C; Chillon JM; Hoffman M; Nicolas JP; Atkinson J

Br J Pharmacol May 1992, 106 (1) p79-84,

1. The haemodynamic effects of S 12968 ( ), a new dihydropyridine calcium entry blocker (enantiomer of S 11568), were compared with those of the stereoisomer, S 12967-(+), nifedipine, and sodium nitroprusside. 2. A first experiment was performed in conscious, young male rats chronically implanted with femoral artery and vein cannula and repeated in rats previously treated with vitamin D3 and nicotine. Such treatment produces marked vascular calcium overload, especially of the compliance arteries, with no overt sign of toxicity as far as can be judged from the plasma profile. 3. In conscious rats the hypotensive effects of S-12968-(-), nifedipine and sodium nitroprusside were of similar potency. The falls in blood pressure produced by nifedipine and sodium nitroprusside were accompanied by reflex tachycardia which was less marked in the vascular calcium overload model. S-12968-(-) did not induce reflex tachycardia. S-12967-(+) increased blood pressure in both models. 4. A second experiment was performed in open chest pentobarbitone-anaesthetized rats with electromagnetic flowprobes on the ascending aorta. In controls the falls in blood pressure produced by low doses (0.1 and 0.3 mg kg-1, i.v.) of S-12968-(-) were accompanied by falls in total peripheral resistance. The higher dose (1 mg kg-1, i.v.) of S-12968-(-) produced no change in total peripheral resistance, and in rats pretreated with vitamin D3 and nicotine, cardiac output fell. 5. In conclusion, S-12968-(-) appears to have a dual action and to lower blood pressure at higher doses at least in part by a cardiac effect.(ABSTRACT TRUNCATED AT 250 WORDS)

5/AU,TI,SO,AB/36 (Item 36 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Smoking cessation in women concerned about weight.

Pirie PL; McBride CM; Hellerstedt W; Jeffery RW; Hatsukami D; Allen S; Lando H

Am J Public Health Sep 1992, 82 (9) p1238-43,

BACKGROUND. Weight gain after smoking cessation is often cited by women smokers as a primary reason for not attempting to quit smoking or for relapsing after a cessation attempt. METHODS. A randomized trial of 417 women smokers was conducted to test the addition of two weight control

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strategies to a smoking cessation program. Participants received the standard smoking cessation program, the program plus nicotine gum, the program plus behavioral weight control, or the program plus both nicotine gum and behavioral weight control. Weight and smoking status were measured at the end of treatment and at 6 and 12 months posttreatment. RESULTS. Smoking cessation rates were highest in the group receiving the smoking cessation program plus nicotine gum. Weight gain did not vary by treatment condition, so its effect on relapse could not be examined by group. There was no significant relationship between weight gained and relapse in individuals. CONCLUSIONS. The added behavioral weight control program was attractive to the participants and did not reduce smoking cessation rates. However, it did not produce the expected effect on weight, thereby restricting our ability to examine the effect of weight control on smoking cessation and relapse.

5/AU,TI,SO,AB/37 (Item 37 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Effects of caffeine, nicotine, ethanol and sodium selenite on pancreatic carcinogenesis in hamsters after initiation with N-nitrosobis(2-oxopropyl)amine.

Nishikawa A; Furukawa F; Imazawa T; Yoshimura H; Mitsumori K; Takahashi M
Carcinogenesis Aug 1992, 13 (8) p1379-82,

The modulating effects of caffeine, nicotine, ethanol and sodium selenite on development of N-nitrosobis(2-oxopropyl)-amine (BOP)-initiated pancreatic tumors were investigated. Female Syrian golden hamsters were given s.c. injections of BOP (10 mg/kg body weight) or saline alone once a week for 3 weeks and then administered 2000 p.p.m. caffeine, 25 p.p.m. nicotine, 20% ethanol or 1 p.p.m. sodium selenite in their drinking water for the next 37 weeks. Control animals were given tap water alone after BOP initiation. Only the BOP-treated groups developed pancreatic adenocarcinomas and dysplasias. The multiplicity of pancreatic carcinomas was significantly higher (P less than 0.05) in animals receiving caffeine than in the controls. In addition, caffeine treatment slightly increased the incidence of carcinomas. Nicotine and ethanol also showed tendencies to enhance pancreatic carcinogenesis, although there were statistically no significant differences regarding lesion development. In contrast, sodium selenite administration was associated with a tendency for a decrease in the number of carcinomas and dysplasias. Thus, among these chemicals of obvious significance to human life-style, caffeine enhanced the development of pancreatic tumors when administered during the post-initiation phase in this hamster model.

5/AU,TI,SO,AB/38 (Item 38 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Impact and cost-effectiveness of smoking interventions.

Tsevat J
Am J Med Jul 15 1992, 93 (1A) p43S-47S,

Cigarette smoking is the foremost preventable cause of death in the United States. Along with being a major contributor to lung cancer, chronic obstructive pulmonary disease, and cerebrovascular disease, smoking is one of several modifiable risk factors for coronary artery disease (CAD). The Coronary Heart Disease Policy Model is a computer simulation model of CAD in the United States. Using the model, one can project CAD incidence, prevalence, events, mortality, cost, cost-effectiveness, and gains in life expectancy from various risk factor modifications, including smoking interventions. The model projects that reducing the number of cigarettes

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smoked by 50% would increase the population-wide life expectancy of 35 year-old U.S. citizens by 0.4 year. Eliminating smoking would yield population wide gains of 0.8 year for 35-year-old males and 0.7 year for 35-year-old females. These gains are comparable to those achieved with strict control of cholesterol levels, diastolic blood pressure, or weight. Gains for the smokers themselves would be much greater. On average, 35-year-old male smokers would live 1.2 years longer if they reduced the number of cigarettes smoked by 50%, and 2.3 years longer if they quit smoking. Females 35 years of age would live 1.5 years longer by cutting back by 50% and 2.8 years longer by quitting. These gains are equal to or greater than gains that individuals would realize by reducing serum cholesterol levels of 240-299 mg/dL to 200 mg/dL; controlling mild hypertension; or reducing weight from greater than or equal to 130% ideal body weight to ideal body weight. Gains projected by the Coronary Heart Disease Policy Model are comparable to those forecast by others, who have projected that young adults would gain approximately 0.2-8.7 years by quitting smoking, depending on their smoking history. Two studies have examined the cost-effectiveness of smoking interventions. One found that counseling smokers to quit would cost only $705-988 per year of life saved for males and $1,204-2,050 per year of life saved for females. The second study found that prescribing nicotine gum as an adjunct to counseling would cost only $4,113-6,465 per year of life saved for males and $6,880-9,473 per year of life saved for females. These cost-effectiveness ratios are more favorable than those of most other current healthcare interventions. Smoking cessation would increase population-wide life expectancy by about a year and the life expectancy of a smoker by several years.(ABSTRACT TRUNCATED AT 400 WORDS)

5/AU,TI,SO,AB/39 (Item 39 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Dexfenfluramine. A review of its pharmacological properties and therapeutic potential in obesity [published erratum appears in Drugs 1992 Jul;44(1):8]

McTavish D; Heel RC

Drugs May 1992, 43 (5) p713-33,

Dexfenfluramine stimulates serotoninergic activity by inhibiting serotonin reuptake into presynaptic neurons and by enhancing its release into brain synapses. Based on the serotonin hypothesis of appetite control these effects would be expected to reduce food intake and thus body-weight. Studies in animal models and severely overweight patients have confirmed the effectiveness of dexfenfluramine as a weight-reducing agent which appears to be well tolerated. Permanent weight loss is the goal of weight-reducing strategies and, based on current clinical evidence, dexfenfluramine appears to exert a weight reducing effect over periods of up to 12 months without development of tolerance, a problem that has limited the long term use of other pharmacological agents used in the treatment of this disorder. Dexfenfluramine facilitated weight loss in patients who had not responded satisfactorily to other weight-reducing strategies, prevented relapse in those patients who had achieved weight reduction by other methods, and corrected disturbed eating patterns (and therefore reduced weight gain) in small studies involving patients with premenstrual syndrome, seasonal affective disorder and nicotine withdrawal syndrome. Follow-up of the longest study reported with dexfenfluramine suggests that continued therapy is required in severely overweight patients if weight loss is to be maintained. Dexfenfluramine has not been directly compared with nonpharmacological measures of weight control such as behaviour modification or exercise programmes. The decision that pharmacological means are indicated in overweight patients must be highly

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individualised, and must consider the many complex factors that often contribute to overweight states, as well as the anticipated magnitude of drug effect. Despite such a cautionary note, and the expected need (at this stage of its development) for an expanded clinical study programme in certain areas, dexfenfluramine is a clear advance in the pharmacological approach to improved management of overweight individuals.

5/AU,TI,SO,AB/40 (Item 10 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Is there a connection between carbon monoxide exposure and hypertension?
Penney DG; Howley JW
Environ Health Perspect Nov 1991, 95 p191-8,

Exposure to carbon monoxide in our society is a frequent occurrence, from auto exhaust, industrial effluents, and cigarette smoke, and takes place over a wide range of concentrations. It has been suggested that chronic CO inhalation may alter blood pressure, even possibly provoking hypertension by acting alone or in combination with other environmental stressors. Some studies examining the response to CO exposure have reported decreases in blood pressure, whereas others have found increases or no change. Blood pressure in long-term cigarette smokers is generally decreased relative to nonsmokers, albeit a slight decrease. The strength of this finding is somewhat clouded by the effect of the lower body weight in smokers. The increases in blood pressure observed acutely with smoking are mainly due to nicotine. Chronically, the hypertensive action of nicotine is largely offset by the hypotensive action of CO. Several studies support the notion that environmental CO exposure or smoking accelerates or exacerbates hypertension in some people. It has been asserted that chronic CO exposure increases the development of atherosclerotic disease; however, convincing evidence from animal experiments is lacking. Nevertheless, CO may elevate plasma cholesterol and does appear to enhance atherosclerosis when serum cholesterol is greatly elevated by diet. Using the borderline hypertensive rat, an animal model reputed to have increased sensitivity to environmental stimuli, we found no evidence to suggest a provocatory role for CO in the development of hypertension; instead, CO exposure produced hypotension. On the whole, the human and animal literature, as well as our studies, fail to support the hypothesis that long-term CO exposure is capable of provoking an increase in blood pressure, even in borderline hypertensive or sensitive individuals.

5/AU,TI,SO,AB/41 (Item 41 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Chronic treatment with the angiotensin I converting enzyme inhibitor, perindopril, protects in vitro carbachol-induced vasorelaxation in a rat model of vascular calcium overload.
Henrion D; Chillon JM; Capdeville-Atkinson C; Vinceneux-Feugier M; Atkinson J
Br J Pharmacol Dec 1991, 104 (4) p966-72,

1. Treatment of young rats with vitamin D3 plus nicotine produced 31 and 4 fold increases in the calcium content of the aorta and the mesenteric arterial bed, respectively. 2. Aortic rings and perfused mesenteric arterial beds from vitamin D3/nicotine-treated animals showed a diminished contractile response to noradrenaline in vitro. 3. In vascular preparations from vitamin D3/nicotine-treated animals, precontracted with noradrenaline, relaxation by the endothelium dependent vasodilator, carbachol, was attenuated but responses to sodium nitroprusside were not modified. 4. Prolonged treatment with the angiotensin I converting enzyme inhibitor,

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perindopril, at a dose (1 mg kg 1) which did not significantly modify blood pressure, failed to prevent vascular calcium overload. 5. Perindopril treatment diminished noradrenaline evoked vasoconstrictor responses of aortic rings in both groups, but restored responses in mesenteric arterial beds of vitamin D3/nicotine treated rats. 6. Perindopril treatment also restored the maximal responses to carbachol of both aortic rings and mesenteric arterial beds of vitamin D3/nicotine-treated rats. 7. In conclusion, in the vitamin D3 plus nicotine model of calcium overload, reduced endothelial mediated relaxation can be prevented by perindopril treatment.

5/AU,TI,SO,AB/42 (Item 42 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Antinociceptive effect of chronic nicotine and nociceptive effect of its withdrawal measured by hot-plate and tail-flick in rats.
Yang CY; Wu WH; Zbuzek VK
Psychopharmacology (Berl) 1992, 106 (3) p417-20,
Nicotine (6 mg/kg/day) was administered subcutaneously via Alzet osmotic pumps to rats for 20 days. Nociception was measured by the hot-plate and tail-flick methods. A significant antinociceptive effect was demonstrated during the first week of the treatment; after that tolerance developed, lasting for the remaining period of nicotine treatment. This effect was more pronounced in the habituated, rather than in the naive, rats. Rats subjected to nicotine withdrawal tended to exhibit the nociceptive effect for 10 days with an overall P value on the border of significance. This chronic nicotine-induced antinociception and nicotine withdrawal-induced nociception was detectable only by hot-plate but not the tail-flick technique.

5/AU,TI,SO,AB/43 (Item 43 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Metabolic effects of cigarette smoking.
Perkins KA
J Appl Physiol Feb 1992, 72 (2) p401-9,
The inverse relationship between cigarette smoking and body weight, a potent obstacle to stopping smoking, may be due in part to effects of smoking on increasing whole body metabolism. Studies examining chronic and acute metabolic effects of smoking, as well as its constituent nicotine, are reviewed. Evidence suggests the absence of a chronic effect; most studies indicate that smokers and nonsmokers have similar resting metabolic rates (RMR) and that RMR declines very little after smoking cessation. Although an acute effect due to smoking is apparent, its magnitude is inconsistent across studies, possibly because of variability in smoke exposure or nicotine intake. In smokers at rest, the acute effect of smoking (and nicotine intake) appears to be significant but small (less than 10% of RMR) and transient (less than or equal to 30 min). However, the specific situations in which smokers tend to smoke may mediate the magnitude of this effect, inasmuch as smoking during casual physical activity may enhance it while smoking after eating may reduce it. Sympathoadrenal activation by nicotine appears to be primarily responsible for the metabolic effect of smoking, but possible contributions from nonnicotine constituents of tobacco smoke and behavioral effects of inhaling may also be important. Improved understanding of these metabolic effects may lead to better prediction and control of weight gain after smoking cessation, thus increasing the likelihood of maintaining abstinence.

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5/AU,TI,SO,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:(c) format only 1991 Dialog Info.Svcs. All rts. reserv.

Effects of dose, gender, and level of physical activity on acute metabolic response to nicotine.
Perkins KA; Epstein LH; Sexton JE; Stiller RL; Jacob RG
Pharmacol Biochem Behav Oct 1991, 40 (2) p203-8,

The acute thermogenic effect of nicotine was examined in cigarette smokers under conditions of rest and two levels of low-intensity physical activity comparable to that normally engaged in by sedentary adults. Male and female smokers (n = 10 each) each received 0 (placebo), 7.5, 15, or 30 micrograms/kg nicotine via measured-dose nasal spray once every 30 min for 90 min, with each dose presented on a separate occasion. After each dose presentation, subjects engaged in 10 min of rest or low-intensity activity at 30 or 60 watts (W) using a bicycle ergometer. For males, results indicated that expenditure attributable to nicotine was more than twice as large during 60-W activity compared with rest, while that during 30-W activity was intermediate. For females, expenditure attributable to nicotine was generally similar to that of males during rest and 30-W activity but was significantly lower during 60-W activity, indicating an apparent "inverted-U" relationship with activity intensity. The enhanced effect of nicotine was specific to energy expenditure, since heart rate showed dose-dependent changes that were generally similar regardless of activity level. These findings confirm a mediating influence of physical activity level on the acute metabolic effect of nicotine, especially in males, and may have implications for explaining individual differences in body weight changes due to tobacco smoking and cessation.

5/AU,TI,SO,AB/45 (Item 45 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Effects of tobacco smoking on caloric intake.
Perkins KA
Br J Addict Feb 1992, 87 (2) p193-205,

Reduced body weight due to smoking may be an important factor inhibiting smoking cessation and promoting relapse after cessation in some smokers. It is popularly believed that smoking decreases body weight by suppressing appetite. However, cross-sectional studies show that, despite their lower body weights, smokers do not eat less than non-smokers or ex-smokers and, in fact, tend to eat slightly more. Similarly, laboratory studies show no acute effects of smoking or nicotine intake via other means on caloric intake in smokers, although intake of non-smokers may be reduced after nicotine. In contrast, longitudinal studies show that eating consistently increases in the first weeks after stopping smoking, but may recede to pre-cessation levels with longer-term abstinence, while resumption of smoking after cessation is accompanied by a reduction in eating. A similar pattern of results is seen for self-reported hunger and some, but not all, constituents of diet. Thus, there appear to be no acute or chronic effects of smoking on eating in smokers maintaining regular smoking, but changes in eating are observed concomitant with changes in smoking status (i.e. cessation or relapse). Although tolerance to anorectic effects of nicotine is one potential explanation, these findings may be more parsimoniously explained by viewing changes in eating due to smoking as secondary to an alteration in the set point around which body weight is regulated. According to this notion, cessation is accompanied by increased eating only until a new, higher body weight set point is reached, while relapse (and perhaps initiation of smoking) decreases eating only until a lower set point is reached. Implications of these findings and a set point explanation for them are discussed.

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5/AU,TI,SO,AB/46 (Item 46 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Nicotine effects on body weight: a regulatory perspective.
Schwid SR; Hirvonen MD; Keesey RE
Am J Clin Nutr Apr 1992, 55 (4) p878-84,

Rats infused with nicotine were initially hypophagic and lost weight. Although food intake recovered, body weight remained 8-12% below normal. Elevating (or reducing) body weight before treatment prolonged (or shortened) initial hypophagia; weight reliably stabilized at the reduced level. At this reduced weight, the treated rats' daily resting energy expenditure was comparable with that of normal-weight controls (262.3 vs 261.9 kJ.d-1.kg body wt-0.75). Reducing the weight of controls to that of treated rats caused their expenditure to drop to 250.6 kJ.d-1.kg body wt-0.75, an energy-conserving adjustment that treated rats also displayed when their weight was lowered from its already-reduced level. Terminating nicotine treatment led initially to hyperphagia, which abated upon body weight being restored to normal. Normal daily energy expenditures at reduced weights suggest that nicotine lowers regulated body energy. Acute intake adjustments associated with initiation (or cessation) of nicotine treatment can be viewed as responses appropriate to bringing body energy into balance with the altered regulation level.

5/AU,TI,SO,AB/47 (Item 47 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

The clinician's role in promoting smoking cessation among clinic patients.
Manley MW; Epps RP; Glynn TJ
Med Clin North Am Mar 1992, 76 (2) p477-94,

Like other chronic conditions, nicotine dependence offers both challenges and rewards to clinicians. The treatment of this condition frequently requires experience in pharmacology, behavioral science, and social aspects of medicine. Physicians are uniquely qualified to assist patients in their efforts to overcome the multifaceted condition of tobacco addiction. In providing this treatment, the clinical challenges are far outweighed by the benefit to patients who stop smoking. For many patients, smoking cessation is, by far, the most important step they can take to improve their health and increase their life span. Physicians who help patients accomplish this difficult goal provide a life-saving service. There is sufficient scientific evidence to guide physicians in their approach to smoking patients. Brief, systematic interventions have been shown to increase patient smoking cessation rates. The intervention can be described in four steps: ask about smoking, advise smokers to stop, assist those who want to stop, and arrange adequate follow up. These interventions are used consistently when a smoking cessation program is adopted by an entire office practice. The components of this office-based program include defining staff roles, maintaining a smoke-free office, stocking appropriate materials, making use of the medical record to identify smokers and to remind staff to intervene, and monitoring patient progress. The potential public health impact of physician intervention with smoking patients is enormous. Even with very modest expectations of cessation rates, 100,000 physicians using effective intervention can produce over 3 million new ex-smokers in the United States each year. In conjunction with other community-based tobacco control efforts, this physician-lead effort will result in a marked reduction in the morbidity and mortality caused by smoking and, thus, control of "the most important public health issue of our time."

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5/AU,TI,SO,AB/48 (Item 48 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Neonatal nicotine exposure induces permanent changes in brain nicotinic receptors and behaviour in adult mice.
Nordberg A; Zhang XA; Fredriksson A; Eriksson P
Brain Res Dev Brain Res Nov 19 1991, 63 (1-2) p223-7,
The effects of neonatal nicotine exposure on spontaneous and nicotine-induced behaviour in 4 month old mice and on the development of brain nicotinic receptors were studied. The behaviour study showed that mice treated with nicotine 66 micrograms ( )nicotine base/kg body weight (bw) s.c. twice daily between 10 and 16 days postnatally displayed a hypoactive condition, whereas mice treated with saline displayed a hyperactive condition. When the nicotinic receptors in the brain cortex were analyzed, the displacement curves for [3H]nicotine(-)nicotine revealed an almost equal proportion of high- and low-affinity binding sites in 17-day-old mice, while the high affinity sites predominated in 4-month-old mice, with affinity constants for both high- and low-affinity binding sites 10 times higher in 4-month old mice than in 17-day-old-mice. A decrease in the number of nicotinic receptors was observed from day 17 to 4 months, mainly of the low affinity nicotinic type. Interestingly, the displacement curves in neonatally nicotine treated mice showed only one population of high-affinity binding sites in 17-day- and 4-month-old mice though the total binding sites in 4-month-old mice were the same for the neonatally nicotine-treated and saline-treated mice. These results indicate that neonatal nicotine treatment prevents the development of low-affinity nicotinic sites in the brain and this earlier exposure to nicotine induces a different behaviour response in adult animals to a test dose of nicotine. Days 10-16 postnatally appear to be a critical period for the effects of nicotine on the brain.

5/AU,TI,SO,AB/49 (Item 49 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Teratogenic effects of nicotine on first molar odontogenesis in the mouse.
Saad AY; Gartner LP; Blatt JL
Acta Morphol Hung 1991, 39 (2) p97-96,
Fetuses of pregnant CD-1 Swiss albino mice, exposed to 0.1% nicotine sulphate at a dose of 1.67 mg/kg body weight from the 6th to the 15th gestational day, were compared with control fetuses to assess the effects of nicotine on first molar odontogenesis. Mothers were sacrificed on the 18th day of gestation. The 130 nicotine treated fetuses, as well as the 348 control fetuses were embedded in paraffin and sectioned in the frontal plane. The developing molars of the experimental fetuses were retarded, less differentiated, and reduced in breadth in comparison with controls. The developing molars of the control fetuses were in the bell stage of odontogenesis, whereas those of the experimental population were either in the late cap or early cap stage, depending on the absence or presence of palatal cleft, which occurred in 9.6% of the fetuses. It is suggested that nicotine, or its metabolic byproducts, interfere with normal interaction between the epithelial and mesenchymal components of the developing tooth.

5/AU,TI,SO,AB/50 (Item 50 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Effects of nicotine on hunger and eating in male and female smokers.
Perkins KA; Epstein LH; Sexton JE, Solberg-Kassel R; Stiller RL; Jacob RG

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Psychopharmacology (Berl) 1992, 106 (1) p53-9,

We tested whether the inverse relationship between smoking and body weight may be due in part to nicotine's acute effects on reducing hunger and eating. On four mornings, male and female smokers (n = 10 each), abstinent overnight from smoking and food, received one of three nicotine doses (7.5, 15, and 30 micrograms/kg) or placebo (0) via nasal spray every 30 min for 2 h. Self reported hunger and satiety ("fullness") and craving for cigarettes were obtained after each dose presentation. Subjects subsequently ate ad lib from a large array of food items varying in sweet taste and fat content. For both males and females, nicotine had no effect on self-reported hunger, but cigarette craving was decreased. Rather than being decreased, caloric intake during the meal was unexpectedly increased following nicotine compared with placebo. Cigarette craving increased after the meal, and this increase was unaffected by nicotine dose. There were virtually no differences between males and females in any effects of nicotine. These results indicate that nicotine may not acutely suppress appetite in fasting smokers and suggest that other actions of nicotine or smoking may account for the lower body weights of smokers.

5/AU,TI,SO,AB/51 (Item 51 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Effect of chronic treatment with the calcium entry blocker, isradipine, on vascular calcium overload produced by vitamin D3 and nicotine in rats.

Henrion D; Chillon JM; Capdeville Atkinson C; Atkinson J

J Pharmacol Exp Ther Jan 1992, 260 (1) p1-8,

Treatment of young rats with vitamin D3 and nicotine produced a 35-fold increase in the calcium content of the aorta and a 4-fold increase in the calcium content of the mesenteric arterial bed. Blood pressure was not modified. In vitro, aortic rings and mesenteric arterial bed preparations from such animals showed diminished vasoconstrictor responses to norepinephrine. After precontraction with norepinephrine, the endothelium dependent vasodilator, carbachol, produced vasorelaxation. This latter effect was attenuated in aortic rings and mesenteric arterial bed preparations from animals previously treated with vitamin D3 and nicotine, but the vasodilator effect of sodium nitroprusside (which is independent of the endothelium) was unchanged. Prolonged treatment with the calcium entry blocker, isradipine, at a dose (1 mg/kg, i.p.) which had no effect on blood pressure, prevented calcium overload of the mesenteric arterial bed, but did not modify aortic calcium overload. Isradipine treatment had no effect on vasoconstrictor responses to norepinephrine in vitro. Such treatment did, however, restore the endothelium-dependent vasodilator effect of carbachol in the mesenteric arterial bed (but not in aortic rings). In conclusion, in a rat model of vascular calcium overload produced by administration of vitamin D3 plus nicotine, chronic treatment with a low dose of the calcium entry blocker, isradipine, restored the endothelium-dependent vasorelaxant effect of carbachol in the mesenteric arterial bed, but not in the aorta.

5/AU,TI,SO,AB/52 (Item 52 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Effects of cannabis and tobacco on the enzymes of alcohol metabolism in the rat.

Marselos M; Vasiliou V; Malamas M; Alikaridis F; Kefalas T

Rev Environ Health 1991, 9 (1) p31-7,

The effects of cannabis and tobacco on the enzymes of ethanol metabolism were studied in the Wistar rat. The activities of alcohol dehydrogenase

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(ADH) and aldehyde dehydrogenase (AlDH) were measured in the liver and the brain, after treatment with an extract of cannabis resin, with an extract of tobacco leaves, or with nicotine. A condensate of cannabis resin extract was collected in a smoking machine, using a tobacco cigarette as the vehicle. Unsmoked or smoked cannabis extracts were dissolved in olive oil and were given i.p. (twice daily, for 7 days). In both cases, a similar dose level was used in terms of starting material (raw cannabis resin), estimated at about 100 mg/kg body weight. Control animals were treated either with olive oil, or with the same amount of smoked condensate obtained from a reference cigarette. Nicotine was dissolved in olive oil and it was given i.p. (10 micrograms/kg, twice daily for 7 days). An extract of unsmoked tobacco was dissolved in olive oil and was given with the same schedule, at a dose which was estimated to correspond to about 10 micrograms nicotine/kg b.w. All groups of animals received an additional i.p. injection on day 8, one hour before sacrifice. Our results showed that unsmoked cannabis inhibited the hepatic activities of the microchondrial AlDH (low-Km and high-Km), the hepatic low-Km cytosolic AlDH (p less than 0.001), and the low-Km mitochondrial AlDH of the brain (p less than 0.001). Administration of smoked cannabis to the animals inhibited the hepatic mitochondrial low-Km AlDH (p less than 0.001), but it did not influence the brain enzymes.(ABSTRACT TRUNCATED AT 250 WORDS)

5/AU,TI,SO,AB/53 (Item 53 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Chronic nicotine treatment intensifies gastric ulceration by cold-restraint stress in rats.

Qiu BS; Cho CH; Ogle CW

Agents Actions Jul 1991, 33 (3-4) p367-70,

Nicotine 5, 25 or 50 micrograms/ml drinking water given ad lib for 5, 10 or 20 days, dose and time-dependently worsened cold-restraint-induced (stress) ulceration in rat stomachs. Treatment with nicotine 5 or 25 micrograms/ml did not influence the number of gastric mucosal mast cells degranulated by cold and restraint; however, drinking 50 micrograms/ml for 10 days lowered further the mast cell count in stressed animals. During 20-day nicotine administration, the daily food intake and body weight gain, up to the 18th day when the animals were starved before experiments, were not affected by the three concentrations of the alkaloid, except that fluid consumption tended to be less only in those animals given the highest dose. The findings indicate that chronic nicotine treatment exacerbates the severity of stress-evoked ulcer formation. The ulcer-intensifying mechanism of the two lower doses of nicotine appears not to be related to additional mast cell degranulation; only the ulcerogenic action of the highest concentration includes this factor. It is unlikely that ulcer aggravation by nicotine is due to malnutrition because body weight gain and solid food intake by the alkaloid-treated rats were normal.

5/AU,TI,SO,AB/54 (Item 54 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Decrease in endothelium-dependent relaxation in the mesenteric arterial bed following vascular calcium overload produced by vitamin D3 and nicotine in rats.

Henrion D; Chillon JM; Hoffman M; Capdeville-Atkinson C; Atkinson J

Life Sci 1991, 49 (8) p575-86,

Treatment of young rats with vitamin D3 plus nicotine, which has been proposed as a model of cardiovascular calcium overload, produced an increase in the calcium content of the mesenteric arterial bed and lowered

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in vitro vasoconstrictor responses to norepinephrine and serotonin. Attenuation of the vasoconstriction induced by norepinephrine by the endothelium-dependent vasodilators, carbachol and histamine, was diminished, but the effects of sodium nitroprusside and papaverine were unchanged. The vitamin D3 plus nicotine model may be useful for the study of the involvement of calcium overload in vascular endothelial dysfunction.

5/AU,TI,SO,AB/55 (Item 55 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Beneficial effects of nicotine.
Jarvik ME
Br J Addict May 1991, 86 (5) p571-5,

Nicotine in tobacco brings illness and death to millions of people. Yet nicotine in its pure form has the potential to be a valuable pharmaceutical agent. Nicotine fairly specifically binds to the cholinergic nicotinic gating site on cationic ion channels in receptors throughout the body. This action stimulates the release of a variety of neurotransmitters including especially catecholamines and serotonin. When chronically taken, nicotine may result in: (1) positive reinforcement, (2) negative reinforcement, (3) reduction of body weight, (4) enhancement of performance, and protection against; (5) Parkinson's disease (6) Tourette's disease (7) Alzheimers disease, (8) ulcerative colitis and (9) sleep apnea. The reliability of these effects varies greatly but justifies the search for more therapeutic applications for this interesting compound.

5/AU,TI,SO,AB/56 (Item 56 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Implications of tobacco use as an addiction [editorial]
West R; Grunberg NE
Br J Addict May 1991, 86 (5) p685-8,

5/AU,TI,SO,AB/57 (Item 57 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Pre- and post-conceptional tobacco effects on the CD-1 mouse fetus.
Paulson RB; Shanfeld J; Krause L; Iranpour S; Paulson JO
J Craniofac Genet Dev Biol Jan-Mar 1991, 11 (1) p48-58,

The objective of this study was to examine the effect of subchronic administration of an aqueous extract of smokeless tobacco (ST) on the development of the CD-1 mouse fetus. Mice were administered ST for approximately 5 weeks: for 2 weeks prior to breeding, during breeding, and during gestational days 0 to 17. Thus the initial peak nicotine levels occurred prior to breeding and not during the critical periods of gestation. Two ST dosages were administered by gastric intubation three times daily: ST/D-1, equivalent to a dose of 12 mg nicotine/kg of body weight, and ST/D-2, equivalent to 20 mg nicotine/kg body weight. Maternal plasma nicotine levels were determined 30 min after the second intubation during the pretreatment and gestational phases of treatment. At these ST dosages, the weight gain of ST-treated dams was not significantly affected in comparison to treated controls. The mean maternal plasma nicotine level for the low-dosage group was 363 ng/ml, and 481 ng/ml for the high-dosage group, with maternal lethality observed at 9.6% and 28.2%, respectively. No significant differences were seen between control and ST/D-1 maternal and/or fetal values, except for placental weights which were heaviest in the ST group (P less than 0.05). Several differences were noted between the

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ST/D-2 group and control: fetal weights were reduced by 5.4% (P less than 0.05); decreased ossification was seen in femur measurements and in nine of ten characteristics measured (P less than 0.05); the frequency of resorptions (7.6%) was almost doubled (controls 4.2%); and the frequency of deaths and malformations was not affected. Under these experimental conditions, the low dose produced a negligible effect on the CD-1 mouse fetus and the dam. The high dose demonstrated growth retardation (P less than 0.05), increased embryotoxicity, and a significant decrease in ossification (P less than 0.05).

5/AU,TI,SO,AB/58 (Item 58 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

[Nutrition-related risk factors in the elderly]
Ernahrungsbedingte Risikofaktoren im Alter.
Nussel E
Zentralbl Hyg Umweltmed Mar 1991, 191 (2-3) p333-46,

In industrialized countries life expectancy in the elderly is decreased mainly by degenerative cardiovascular diseases such as myocardial infarction and stroke. Nutrition, especially excessive intake of calories, unbalanced diets as well as abuse of alcohol and nicotine play an important role in cardiovascular mortality and morbidity just as these factors do in the pathogenesis of certain types of cancer. The National Health Survey 1984/86 in the FRG offers data on the prevalence of such risk factors as elevated body weight, elevated blood pressure, hypercholesterolaemia, cigarette smoking and alcohol consumption in different age groups. This knowledge provides the basis of modern primary health care and health education in order to limit diseases caused by unhealthy nutrition. In this respect the countrywide integrated programme for action called "7 against 7" is not just an important part of primary health care carried out by general practitioners but also an effective instrument in the fight against civilization diseases.

5/AU,TI,SO,AB/59 (Item 59 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

A double-blind trial of a 16-hour transdermal nicotine patch in smoking cessation [see comments]
Tonnesen P; Norregaard J; Simonsen K; Sawe U
N Engl J Med Aug 1 1991, 325 (5) p311-5,

BACKGROUND. The use of nicotine chewing gum combined with psychological support improves the success rate in quitting smoking. We studied the safety and efficacy of a transdermal nicotine patch in smoking cessation. METHODS. We conducted a double blind randomized study comparing the effects of a 16-hour nicotine patch (15 +/- 3.5 mg of nicotine in 16 hours) with those of a placebo patch. Of the 289 smokers (207 women and 82 men) enrolled in the study, 145 were treated with nicotine patches and 144 with placebo patches for 16 weeks. RESULTS. Rates of sustained abstinence were significantly better with active treatment than with placebo: 53, 41, 24, and 17 percent of those in the nicotine-patch group were abstinent after 6, 12, 26, and 52 weeks, respectively, as compared with 17, 10, 5, and 4 percent of those in the placebo-patch group (P less than 0.0001). Only two subjects with the nicotine patch and one with the placebo patch had to withdraw from the study because of side effects. CONCLUSIONS. The nicotine skin patch proved to be safe and effective, as demonstrated by a higher rate of abstinence than with placebo. However, the absolute rate of abstinence after one year was only 17 percent, which is lower than the rate in studies that have combined the use of nicotine chewing gum with

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behavioral therapy.

5/AU,TI,SO,AB/60 (Item 60 from file: 155)
DIALOG(R)File 155:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

Acute effects of nicotine on hunger and caloric intake in smokers and nonsmokers.

Perkins KA; Epstein LH; Stiller RL; Fernstrom MH; Sexton JE; Jacob RG; Solberg R

Psychopharmacology (Berl) 1991, 103 (1) p103-9,

The inverse relationship between smoking and body weight may be due in part to nicotine's effects on reducing hunger and eating. Male smokers and nonsmokers (n = 10 each), abstinent overnight from smoking and food, participated in four sessions, involving consumption of a liquid caloric load or water followed by nicotine (15 micrograms/kg) or placebo via nasal spray every 20 min for 2 h. Hunger and satiety ("fullness") ratings were obtained prior to each dose presentation. At the end of the two sessions involving the caloric load (simulating breakfast), subjects were also presented with typical lunch/snack food items varying in sweet taste and fat content for ad lib consumption. Results indicated that, for both smokers and nonsmokers, the hunger reducing effects of nicotine occurred only following caloric load consumption, and there was no effect of nicotine on hunger afer water consumption. Smokers unexpectedly reported greater satiation than nonsmokers following the caloric load regardless of nicotine or placebo condition. Nicotine also resulted in less caloric intake during the meal, and the decrease was not specific to consumption of sweet, high-fat foods. These results indicate that nicotine reduces appetite, possibly helping to explain the influence of smoking on body weight.

5/AU,TI,SO,AB/61 (Item 1 from file: 5)
DIALOG(R)File 5:(c) 1994 BIOSIS. All rts. reserv.

Prenatal smokeless tobacco effects on the rat fetus

Paulson R B; Shanfeld J; Mullet D; Cole J; Paulson J O

Journal of Craniofacial Genetics and Developmental Biology 14 (1). 1994. 16-25.

Full Journal Title: Journal of Craniofacial Genetics and Developmental Biology

The objective of this study was to examine the effect of an aqueous extract of smokeless tobacco (ST) on the development and bone ossification of the Sprague Dawley rat fetus at known nicotine blood levels. Dams were intubated with the ST extract three times daily on gestational days (GD) 6-18 with one of the following: ST equivalent to either 1.33 mg nicotine/kg body weight (STD-1), 6 mg nicotine/kg body weight (STD-2), or equal amounts of distilled water (sham treated controls). Parallel groups of rats were used for nicotine-blood-level determinations. Dams were killed on GD 19, fetuses and placentas were weighed, and resorptions, deaths, and/or malformations were noted. Two thirds of the fetuses were further examined by Wilson's method, and the remaining one third was stained and cleared for skeletal examinations. Mean plasma nicotine levels, determined in a parallel group of nonpregnant/pregnant rats, were 220.4/283.3 ng/ml in the STD-1 group and 869.1/846.3 ng/ml in the STD-2 group. At these ST dosages, weight gain of dams was reduced in comparison with sham-treated controls (P lt .05), but fetal weights were reduced in the STD-2 group only. Placental weights, litter size, resorptions, deaths, and malformations were not significantly affected. Skeletal examinations revealed several dose-related differences between the ST treated and sham-treated control groups. In the

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STD-1 group, reductions in ossification were seen in the nasal and femur width measurements only. In the STD-2 group, reductions in ossification were seen in femur length and width, in the number of ossification centers in the forelimb, in the maxillary, mandibular, and nasal bone measurements. We conclude that under these experimental conditions the effects of ST at the low dose are minimal, whereas the high ST dose resulted in significant growth retardation and decreased ossification levels (P lt .05).

5/AU,TI,SO,AB/62 (Item 2 from file: 5)
DIALOG(R)File 5:(c) 1994 BIOSIS. All rts. reserv.

Smoking and food intake in a field study: Continuous actometer-heart rate recording and pocket computer assisted dietary reports, subjective self-assessments, and mental performance

Baettig K; Kos J; Hasenfratz M

Drug Development Research 31 (1). 1994. 59-70.

Full Journal Title: Drug Development Research

Four-day food intake reports, collected with electronic diaries, and saliva probes for cotinine analysis were obtained from 39 smokers and 43 nonsmokers. The nonsmokers had a higher caloric intake than the smokers, but this was related to more frequent sport activities. The distribution of energy intake across carbohydrates, fat, and protein was identical for both groups, but the smokers consumed bread, sweets and desserts, cheese, fruit juices, muesli (a cereal and yoghurt mixture), and water less frequently, but also more soft drinks, coffee, and alcohol. Only coffee and alcohol drinking were correlated with saliva cotinine. For two additional days, the recording of food intake was continued together with the continuous recording of activity and heart rate, intermittent measurements of blood pressure, assessments of subjective state, and performing a mental task. On one of these 2 days, the smokers had to abstain from smoking. Abstinence lowered heart rate and increased caloric intake by about 500 kcal, whereas actometer readings, blood pressure, subjective state, and mental performance were unaffected. Also unaffected were the percentage intake of fat, protein, and carbohydrates and the frequency of consuming particular food items. Post hoc correlations between subjective state, cotinine measures, excess intakes of total calories, macronutrients, and specific groups of food items were obtained only occasionally and in an inconsistent fashion. It is suggested that effects of smoking on taste and eating as a hedonic substitute when abstaining might represent important factors for food intake beyond the effects of nicotine. The new methods developed for this study appear to offer a way to obtain detailed information under particularly naturalistic conditions in studies on smoking and related problems.

5/AU,TI,SO,AB/63 (Item 3 from file: 5)
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The early chick embryo as a model to evaluate cardiovascular effects of adrenaline and nicotine

Rosenbruch M; Kniepen J; Weishaupt C

Toxicology In Vitro 7 (4). 1993. 541-545.

Full Journal Title: Toxicology In Vitro

During the early stages of development, chick embryos offer a good model for vascular and circulatory studies. The present experiments were carried out with nicotine and adrenaline as validation substances, to test whether this system can be applied to evaluate functional cardiovascular effects. Nicotine was injected into the yolk before incubation and administered topically on different days of incubation. Adrenaline was injected

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intravascularly to evaluate functional effects (heart rate and heart arrhythmia). Mortality rates following nicotine and adrenaline application were determined. An injection of nicotine prior to incubation resulted in a dose-related increase in undeveloped chick embryos, and the topical application led to hyperaemia and haemorrhages. The body weight of the embryos was reduced due to the repeated nicotine application. After iv injection of adrenaline, heart rate increase and the occurrence of heart arrhythmia showed dose-response effects and the mortality rate was three-fold higher as compared with the controls. These results show that, following the application of adrenaline and nicotine, effects on the early chick embryo are similar to those seen in other test systems. In addition to its use in toxicology, this model is suitable for the evaluation of functional cardiovascular effects. The system does not require living animals, and uses stages of development during which the nervous system is still immature.

5/AU,TI,SO,AB/64 (Item 4 from file: 5)
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Increased aortic endothelial cell death and enhanced transendothelial macromolecular transport in streptozotocin-diabetic rats
Lin S-J; Hong C-Y; Chang M-S; Chiang B N; Chien S
Diabetologia 36 (10). 1993. 926-930.
Full Journal Title: Diabetologia

Hypertension, cigarette smoking and diabetes mellitus are well-known risk factors for atherosclerosis and coronary heart disease. Repeated endothelial cell injury and increased lipid entry have been suggested as initiating events in atherogenesis. Our previous studies have demonstrated that the frequency of endothelial cell death and associated endothelial permeability were significantly increased in the aorta of spontaneously hypertensive rats and chronic oral nicotine-treated rats. In the present investigation, we examined the hypothesis that diabetes also increases the frequency of arterial endothelial cell death and hence transendothelial macromolecular transport, which may have some implications in increasing lipid entry and thus accelerating atherogenesis. Diabetes was induced in 15 male Sprague-Dawley rats by intraperitoneal injection of 60 mg streptozotocin per kg body weight. The duration of diabetes was 6 weeks. A group of 15 age-matched rats, injected only with the buffer and maintained over the same time period, served as the controls. In en face preparations of the thoracic aorta, IgG-containing dead endothelial cells were identified by an indirect immunoperoxidase method, and endothelial leakage to Evans blue-albumin complexes was quantified by fluorescence microscopy. Diabetic rats, compared to control rats, had significantly higher values for the frequency of endothelial cell death (0.77 +- 0.10% vs 0.38 +- 0.04%; p lt 0.005 by two-tailed, unpaired Student's t-test) and the number density of Evans blue-albumin leaky foci (4.33 +- 0.48/mm-2 vs 2.99 +- 0.38/mm-2; p lt 0.05 by two-tailed, unpaired t-test) in the aorta. It is concluded that, similar to the situations in hypertension and nicotine consumption, the observed increase in the frequency of endothelial cell death and macromolecular permeability to large molecules in the aorta in streptozotocin-induced diabetic rats suggest that these changes may contribute to accelerated atherogenesis in diabetes.

5/AU,TI,SO,AB/65 (Item 5 from file: 5)
DIALOG(R)File 5:(c) 1994 BIOSIS. All rts. reserv.

DEVELOPMENT OF A NEW NICOTINE TRANSDERMAL DELIVERY SYSTEM IN-VITRO KINETICS STUDIES AND CLINICAL PHARMACOKINETIC EVALUATIONS IN TWO ETHNIC

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Source: https://www.industrydocuments.ucsf.edu/docs/jrdl0000

GROUPS
LIN S; HO H; CHIEN Y W
J CONTROLLED RELEASE 26 (3). 1993. 175-193.
Full Journal Title: Journal of Controlled Release

Nicotine transdermal delivery systems (nicotine-TDSs) have provided effective assistance to smokers in smoking cessation with minimal occurrence of withdrawal symptoms. However, substantial skin reactions have been reported with the four nicotine-TDSs marketed recently. To reduce the skin reactions, a new type of nicotine TDS has been recently developed. In vitro skin permeation studies demonstrated that this nicotine-TDS yields a constant skin permeation profile with a permeation rate of Ø.Ø68 (.+-. Ø.ØØ3) mg/cm2/h across human cadaver skin and Ø.Ø59 (.+-. Ø.Ø14) mg/cm2/h across hairless rat skin, which are comparable to the steady-state permeation rates attained by Habitrol and Nicoderm systems. The clinical pharmacokinetic evaluations in two ethnic groups of smokers indicated that a steady-state nicotine plasma level has been maintained throughout the course of 24-h topical application. While a higher daily dosage of nicotine has been delivered transdermally to Taiwanese smokers, from all three patch sizes, than to American smokers, no clear demographic effect was detected in most pharmacokinetic parameters between these ethnic groups, even after taking the difference in subjects body weight into consideration.

5/AU,TI,SO,AB/66 (Item 6 from file: 5)
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TRANSDERMAL NICOTINE A REVIEW OF ITS PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES AND THERAPEUTIC EFFICACY AS AN AID TO SMOKING CESSATION
PALMER K J; BUCKLEY M M; FAULDS D
DRUGS 44 (3). 1992. 498-529.
Full Journal Title: Drugs

Transdermal nicotine delivery systems are a cigarette smoking cessation aid designed to deliver nicotine into the systemic circulation via the skin. The partial replacement of plasma nicotine, which would have otherwise been obtained from cigarettes, reduces the severity of nicotine withdrawal symptoms, and so allows the smoker to abstain from smoking more easily. The systems are available in 16- and 24-hour application regimens and are recommended for daily use for up to 2Ø weeks, including a series of 'weaning-off' courses. Clinical trials have shown that abstinence rates of 3Ø to 41% can be achieved during the first 6 weeks of applicaiton of transdermal nicotine systems, compared with 4 to 21% with placebo systems. The use of concomitant behavioural therapy may increase the success of treatment, with initial abstinence rates of up to 86% reported. However, long term abstinence rates (> 6 months) are considerably lower with or without behavioural therapy, often falling to less than half of the initial rates. Transdermal nicotine systems have been well tolerated in clinical trials, with local irritation at the site of application being the most common adverse event. Mild gastric, central nervous system (CNS) and sleep disturbances have also been reported. The ease of use and unobtrusive nature of the systems have resulted in a high degree of patient compliance. Thus, transdermal nicotine systems offer a convenient form of nicotine replacement therapy which are well tolerated and, due to their pharmacokinetic profile, probably have a low dependency potential. The short term abstinence rates achieved with this therapy are encouraging, however, the maintenance of abstinence in the long term is harder to achieve. Transdermal nicotine replacement therapy, therefore, represents an important advance in the difficult area of smoking cessation management.

5/AU,TI,SO,AB/67 (Item 7 from file: 5)

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INTERSPECIES SCALING OF NICOTINE CONCENTRATIONS IN THE BRAIN A PHYSIOLOGICALLY BASED PHARMACOKINETIC STUDY
FLOWCHALK D R; DEBETHIZY J D
LIPPIELLO, P. M., ET AL. (ED.). THE BIOLOGY OF NICOTINE: CURRENT RESEARCH ISSUES; CONFERENCE, WINSTON SALEM, NORTH CAROLINA, USA, DECEMBER 1990. XIII+225P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. ISBN 0-88167-860-0. 0 (0). 1992. 55-69.

5/AU,TI,SO,AB/68 (Item 8 from file: 5)
DIALOG(R)File 5:(c) 1994 BIOSIS. All rts. reserv.

PRE-CONCEPTIONAL AND POST-CONCEPTIONAL TOBACCO EFFECTS ON THE CD-1 MOUSE FETUS
PAULSON R B; SHANFELD J; PRAUSE L; IRANPOUR S; PAULSON J O
J CRANIOFACIAL GENET DEV BIOL 11 (1). 1991. 48-58.
Full Journal Title: Journal of Craniofacial Genetics and Developmental Biology
The objective of this study was to examine the effect of subchronic administration of an aqueous extract of smokeless tobacco (ST) on the development of the CD-1 mouse fetus. Mice were administered ST for approximately 5 weeks: for 2 weeks prior to breeding, during breeding, and during gestational days 0 to 17. Thus the initial peak nicotine levels occurred prior to breeding and not during the critical periods of gestation. Two ST dosages were administered by gastric intubation three times daily: ST/D-1, equivalent to a dose of 12 mg nicotine/kg of body weight, and ST/D2, equivalent to 20 mg nicotine/kg body weight. Maternal plasma nicotine levels were determined 30 min after the second intubation during the pretreatment and gestational phases of treatment. At these ST dosages, the weight gain of ST-treated dams was not significantly affected in comparison to treated controls. The mean maternal plasma nicotine level for the low-dosage group was 363 ng/ml, and 481 ng/ml for the high-dosage group, with maternal lethality observed at 9.6% and 28.2%, respectively. No significant differences were seen between control and ST/D-1 maternal and/or fetal values, except for placental weights which were heaviest in the ST group ($P < 0.05$). Several differences were noted between the ST/D-2 group and controls: fetal weights were reduced by 5.4% ($P < 0.05$); decreased ossification was seen in femur measurements and in nine of ten characteristics measured ($P < 0.05$); the frequency of resorptions (7.6%) was almost doubled (controls 4.2%); and the frequency of deaths and malformations was not affected. Under these experimental conditions, the low dose produced a negligible effect on the CD-1 mouse fetus and the dam. The high dose demonstrated growth retardation ($P < 0.05$), increased embryotoxicity, and a significant decrease in ossification ($P < 0.05$).

5/AU,TI,SO,AB/69 (Item 9 from file: 5)
DIALOG(R)File 5:(c) 1994 BIOSIS. All rts. reserv.

EFFECTS OF CHRONIC NICOTINE TREATMENT ON THE IMMOBILIZATION STRESS IN RATS
NISHIO M; KIGOSHI S; MURAMATSU I
64TH ANNUAL MEETING OF THE JAPANESE PHARMACOLOGICAL SOCIETY, KOBE, JAPAN, MARCH 24-27, 1991. JPN J PHARMACOL 55 (SUPPL. 1). 1991. 280P.

5/AU,TI,SO,AB/70 (Item 10 from file: 5)
DIALOG(R)File 5:(c) 1994 BIOSIS. All rts. reserv.

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EFFECT OF MATERNAL ALCOHOL AND NICOTINE INTAKE INDIVIDUALLY AND IN COMBINATION ON FETAL GROWTH IN THE RAT

LEICHTER J

BIOCHEM ARCH 7 (1). 1991. 13-20.

Full Journal Title: Biochemical Archives

The effect of maternal ethanol and nicotine administration, separately and in combination, on fetal growth of rats was studied. Nicotine was administered by gavage (about 3 mg/kg body weight/day) for the entire gestational period. Alcohol was given in drinking water for 4 weeks prior to mating (10% the first week and 20% during the next 3 weeks) and 30% throughout gestation. Appropriate pair-fed and ad libitum control animals were included to separate the effect of ethanol and nicotine on outcome of pregnancy from those produced by the confounding variables of malnutrition. Body weights of fetuses exposed to alcohol alone or in combination with nicotine were significantly lower than those of the pair-fed and ad libitum controls. However, the difference in fetal body weight between the alcohol plus nicotine and the alcohol alone group was not significant. Similarly, in the rats administered nicotine only, fetal weight was not significantly different compared to control animals. The results of this study indicate that maternal alcohol intake impairs fetal growth and nicotine does not, regardless whether it is administered separately or in combination with alcohol for the entire gestational period.

5/AU,TI,SO,AB/71 (Item 11 from file: 5)

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TERATOGENIC EFFECT OF NICOTINE ON PALATE FORMATION IN MICE

SAAD Y A; GARTNER L P; HIATT J L

BIOL STRUCT MORPHOG 3 (1). 1990-1991. 31-36.

Full Journal Title: Biological Structures and Morphogenesis

Fetuses of pregnant CD 1 mice, exposed to intraperitoneal injection of 0.1% nicotine sulfate at a dose of 1.67 mg/kg body weight/day on gestational days 6-15, were compared with control (saline injected and non-injected) fetuses to assess the effects of nicotine on fetal growth in general and palatogenesis in particular. At total of 59 pregnant females (18 experimental and 41 control) were sacrified on the 18th gestational day and their fetuses were examined gross morphologically and histologically (using serial sections through the head in the frontal plane). Data analysis revealed that maternal weight gain, crown-rump length, fetal weight and head dimensions were significantly reduced in nicoted treated animals when compared to those of the controls. Histological examination revealed that 9.6% of fetuses of nicotine injected mothers presented clefts of the palate, whereas none of the control fetuses had that anomaly. It was concluded that nicotine has a determintal effect on general growth and development as well as on palatogenesis of mice.

5/AU,TI,SO,AB/72 (Item 1 from file: 73)

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Acute effects of tobacco smoking on hunger and eating in male and female smokers

Perkins K.A.; Sexton J.E.; Dimarco A.; Fonte C.

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Cigarette smoking is associated with reduced body weight, an effect which has often been attributed to acute anorectic actions of nicotine. In this study, male and female smokers (n=10 each), abstinent overnight from smoking and food, participated in three 2-h sessions, involving intermittent, controlled exposure to their usual cigarette (mean yield

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(0.75mg nicotine), a very low nicotine cigarette (0.1mg) or an unlit cigarette. Hunger and cigarette craving were assessed throughout each session, which ended with ad libitum consumption of a variety of food items ('lunch'). Plasma nicotine analyses confirmed successful control of nicotine exposure via smoking. Results indicated no differences across cigarette conditions in hunger, in contrast to the sharp differences in cigarette craving. There were no differences in total caloric intake, or in macronutrient or taste selection. There were also no differences in any responses to smoking condition as a function of gender. These findings cast into question the commonly held notion that nicotine or smoking has acute anorectic actions in smokers.

5/AU,TI,SO,AB/73 (Item 2 from file: 73)
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Effects of chronic treatment with (+)- and (-) nicotine on nicotinic acetylcholine receptors and N-methyl-D-aspartate receptors in rat brain
Zhang X.; Gong Z.-H.; Nordberg A.
BRAIN RES. , 1994, 644/1 (32-38)

In this study, the effects of chronic treatment with (+)-nicotine on brain nicotinic acetylcholine receptors (nAChRs) and N-methyl-D-aspartate (NMDA) receptors, as well as on animal body weight were compared with those of chronic treatment with nicotine. Male Sprague-Dawley rats were s.c. injected with saline, (+)-nicotine (2.0 mg free base/kg b.w.) or (-)-nicotine (0.45 mg free base/kg b.w.) for 18 days. Brain nAChRs were investigated by (-) (3H)nicotine binding. A significant increase in the high-affinity (-)-(3H)nicotine (5 nM)-binding sites was observed in the cortex, hippocampus, midbrain and striatum but not in the cerebellum of the rats treated with either (+) or (-)-nicotine. The displacement curves of (-)-(3H)nicotine/(-)-nicotine in the cortices of rats treated with either (+)- or (-)-nicotine showed only one population of high-affinity binding sites, whereas both high and low-affinity binding sites were observed in the cortices of control animals. Brain NMDA receptors were studied by (3H)MK-801, which binds to the NMDA receptor-ion channel complex. A significant decrease in the B(max), but not in the K(D) for (3H)MK-801 binding in the cortices of rats treated with either (+)- or (-)-nicotine was only detected under certain experimental conditions where the NMDA receptors seem not to be maximally activated. The body weight of the animals treated with (-)-nicotine was significantly lower than that of the control animals, whereas there was no difference in body weight between (+)-nicotine and saline-treated animals. These results show that (+)-nicotine treatment has an effect on nAChRs in rat brains which is similar to that of (-)-nicotine treatment, but an effect on body weight which differs from (-)-nicotine, and also suggest that nicotinic agonists may interact with brain NMDA receptors in vivo.

5/AU,TI,SO,AB/71 (Item 3 from file: 73)
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Prevalence of hypertension in childhood
PRAVALENZ DER HYPERTONIE IM KINDESALTER
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FORTSCHR. MED. , 1994, 112/5 (31-36)

Background information: Very few studies have been published on the incidence of hypertension in childhood and adolescence, in particular in the doctor's office. Method: In view of this, the Lehrauftrag Allgemeinmedizin at the University of Heidelberg carried out a study in the Northern part of the German State of Baden-Wurttemberg involving 21 general

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practices and 410 children aged between 4 and 18 years. In addition to a questionnaire covering personal, social and family data, the systolic and diastolic blood pressures were determined by automatic oscillometric measurement, and also using a mercury sphygmomanometer. Results: Hypertension was found in 2.93% of the children examined. At the time of diagnosis, half of all the children were suffering from some acute disease; however, more than 10% were discovered 'by accident'. Interesting relationships were found between hypertension, body weight, nicotine and alcohol abuse, sporting activities and family data, which, however, owing to the small number of subjects, were not amenable to more detailed analysis.

5/AU,TI,SO,AB/75 (Item 4 from file: 73)
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Nicotine withdrawal: A behavioral assessment using schedule controlled responding, locomotor activity, and sensorimotor reactivity
Helton D.R.; Modlin D.L.; Tizzano J.P.; Rasmussen K.
PSYCHOPHARMACOLOGY , 1993, 113/2 (205-210)

Three different behavioral measures were used to assess the effects of abrupt cessation of chronic nicotine treatment. Nicotine (0, 3, or 6 mg/kg per day) was continuously administered for 12 days in rats by surgically implanting Alzet osmotic mini pumps subcutaneously. Experiment 1 employed a light/dark discrimination task. There were no significant effects on number of responses or percent correct responding either during nicotine administration, or following cessation of nicotine. Experiment 2 examined ambulatory (locomotor) and nonambulatory activity. Chronic nicotine administration produced significant dose-dependent increases in both ambulatory and nonambulatory activity during the first 3 days of exposure. However, no significant alterations were seen in activity levels following nicotine cessation. Experiment 3 examined sensorimotor reactivity using the auditory startle response. During nicotine withdrawal, significant increases were seen in startle amplitude in both nicotine groups for 4 days. Nicotine (0.4 mg/kg, IP) administered before startle testing during the withdrawal phase attenuated the increased reactivity seen during nicotine cessation. These studies indicate that 1) rats display increased sensorimotor reactivity after cessation of chronic nicotine exposure, and 2) the expression of nicotine dependence and withdrawal is dependent on the behavioral task employed.

5/AU,TI,SO,AB/76 (Item 5 from file: 73)
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Effect of monitored smoking cessation on plasma lipid profiles
Kotamaki M.; Laustiola K.E.
J. SMOK. RELAT. DISORD. , 1993, 4/3 (219-226)

The effect of monitored smoking cessation on plasma fatty acid composition and blood rheology was studied in 10 male subjects. Cessation of smoking was monitored by analysing nicotine metabolites in urine, while haematological and lipid parameters were analysed after three and eight weeks of cessation. We report a significant increase in total cholesterol, HDL and HDL/LDL ratio. Both the weight of the subjects and the body mass index increased significantly. Saturated fatty acids increased significantly after three weeks in the TG fraction and after eight weeks in the cholesteryl ester fraction, implying an effect of dietary alteration. The ratios of unsaturated/saturated and polyunsaturated/saturated fatty acids decreased significantly. There were also significant increases in stearic acid, arachidonic acid and palmitoleic acid, and significant

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